

CLAIMS

1. An reagent for detecting differentiation from hematopoietic stem cell into a monocyte and/or a macrophage,
5 which comprises, as an active ingredient, a substance having binding activity to a human VEGF receptor Flt-1.

2. The reagent according to claim 1, wherein the substance having binding activity to a human VEGF receptor
10 Flt-1 is an antibody against a human VEGF receptor Flt-1.

3. The reagent according to claim 2, wherein the antibody against a human VEGF receptor Flt-1 is a polyclonal antibody or a monoclonal antibody.

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4. The reagent according to claim 3, wherein the monoclonal antibody is an antibody selected from an antibody produced by a hybridoma, a humanized antibody and antibody fragments thereof.

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5. The reagent according to claim 4, wherein the antibody produced by a hybridoma is an antibody selected from the group consisting of KM1730, KM1731, KM1732, KM1748 and KM1750.

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6. The reagent according to claim 4, wherein the humanized antibody is an antibody selected from a human chimeric antibody and a human complementarity determining region-grafted antibody.

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7. The reagent according to claim 6, wherein the human chimeric antibody is KM2532 or KM2550.

8. The reagent according to claim 6, wherein the
10 human complementarity determining region-grafted antibody
is an antibody selected from the group consisting of KM8550,
KM8551, KM8552, KM8553, KM8554 and KM8555.

9. The reagent according to claim 4, wherein the
15 antibody fragment is an antibody fragment selected from the
group consisting of Fab, Fab', F(ab')₂, a single chain
antibody, a disulfide-stabilized Fv and a peptide
comprising a complementarity determining region.

20 10. The reagent according to any one of claims 2
to 9, wherein the antibody is an antibody fused with a
radioisotope, a protein or a low molecular weight agent by
a chemical or genetic engineering means.

25 11. A method for detecting differentiation from
hematopoietic stem cell into a monocyte and/or a macrophage,

which comprises using a substance having binding activity to a human VEGF receptor Flt-1.

12. The method according to claim 11, wherein the
5 substance having binding activity to a human VEGF receptor Flt-1 is an antibody against a human VEGF receptor Flt-1.

13. The method according to claim 12, wherein the antibody against a human VEGF receptor Flt-1 is a
10 polyclonal antibody or a monoclonal antibody.

14. The method according to claim 13, wherein the monoclonal antibody is an antibody selected from an antibody produced by a hybridoma, a humanized antibody and
15 antibody fragments thereof.

15. The method according to claim 14, wherein the antibody produced by a hybridoma is an antibody selected from the group consisting of KM1730, KM1731, KM1732, KM1748
20 and KM1750.

16. The method according to claim 14, wherein the humanized antibody is an antibody selected from a human chimeric antibody and a human complementarity determining
25 region-grafted antibody.

17. The method according to claim 16, wherein the human chimeric antibody is KM2532 or KM2550.

18. The method according to claim 16, wherein the 5 human complementarity determining region-grafted antibody is an antibody selected from the group consisting of KM8550, KM8551, KM8552, KM8553, KM8554 and KM8555.

19. The method according to claim 14, wherein the 10 antibody fragment is an antibody fragment selected from the group consisting of Fab, Fab', F(ab')₂, a single chain antibody, a disulfide-stabilized Fv and a peptide comprising a complementarity determining region.

15 20. The method according to any one of claims 12 to 19, wherein the antibody is an antibody fused with a radioisotope, a protein or a low molecular weight agent by a chemical or genetic engineering means.

20 21. A diagnostic agent for diseases related to a monocyte and/or a macrophage, which comprises, as an active ingredient, a substance having binding activity to a human VEGF receptor Flt-1.

25 22. The diagnostic agent according to claim 21, wherein the disease related to a monocyte and/or a

macrophage is an inflammatory disease, a delayed type hypersensitivity, an arteriosclerosis, or a malignant tumor.

23. The diagnostic agent according to claim 21,
5 wherein the substance having binding activity to a human
VEGF receptor Flt-1 is an antibody against a human VEGF
receptor Flt-1.

24. The diagnostic agent according to claim 23,
10 wherein the antibody against a human VEGF receptor Flt-1 is
a polyclonal antibody or a monoclonal antibody.

25. The diagnostic agent according to claim 24,
wherein the monoclonal antibody is an antibody selected
15 from an antibody produced by a hybridoma, a humanized
antibody and antibody fragments thereof.

26. The diagnostic agent according to claim 25,
wherein the antibody produced by a hybridoma is an antibody
20 selected from the group consisting of KM1730, KM1731,
KM1732, KM1748 and KM1750.

27. The diagnostic agent according to claim 25,
wherein the humanized antibody is an antibody selected from
25 a human chimeric antibody and a human complementarity
determining region-grafted antibody.

28. The diagnostic agent according to claim 27,
wherein the human chimeric antibody is KM2532 or KM2550.

5 29. The diagnostic agent according to claim 27,
wherein the human complementarity determining region-
grafted antibody is an antibody selected from the group
consisting of KM8550, KM8551, KM8552, KM8553, KM8554 and
KM8555.

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30. The diagnostic agent according to claim 25,
wherein the antibody fragment is an antibody fragment
selected from the group consisting of Fab, Fab', F(ab')₂, a
single chain antibody, a disulfide-stabilized Fv and a
15 peptide comprising a complementarity determining region.

31. The diagnostic agent according to any one of
claims 23 to 30, wherein the antibody is an antibody fused
with a radioisotope, a protein or a low molecular weight
20 agent by a chemical or genetic engineering means.

32. A method for diagnosing diseases related to a
monocyte and/or a macrophage, which comprises, as an active
ingredient, using a substance having binding activity to a
25 human VEGF receptor Flt-1.

33. The method according to claim 32, wherein the disease related to a monocyte and/or a macrophage is an inflammatory disease, a delayed type hypersensitivity, an arteriosclerosis, or a malignant tumor.

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34. The method according to claim 32, wherein the substance having binding activity for human VEGF receptor Flt-1 is an antibody against a human VEGF receptor Flt-1.

10 35. The method according to claim 34, wherein the antibody against a human VEGF receptor Flt-1 is a polyclonal antibody or a monoclonal antibody.

15 36. The method according to claim 35, wherein the monoclonal antibody is an antibody selected from an antibody produced by a hybridoma, a humanized antibody and antibody fragments thereof.

20 37. The method according to claim 36, wherein the antibody produced by a hybridoma is an antibody selected from the group consisting of KM1730, KM1731, KM1732, KM1748 and KM1750.

25 38. The method according to claim 36, wherein the humanized antibody is an antibody selected from a human

chimeric antibody and a human complementarity determining region-grafted antibody.

39. The method according to claim 38, wherein the
5 human chimeric antibody is KM2532 or KM2550.

40. The method according to claim 38, wherein the
human complementarity determining region-grafted antibody
is an antibody selected from the group consisting of KM8550,
10 KM8551, KM8552, KM8553, KM8554 and KM8555.

41. The method according to claim 36, wherein the
antibody fragment is an antibody fragment selected from the
group consisting of Fab, Fab', F(ab')₂, a single chain
15 antibody, a disulfide-stabilized Fv and a peptide
comprising a complementarity determining region.

42. The diagnostic method according to any one of
claims 34 to 41, wherein the antibody is an antibody fused
20 with a radioisotope, a protein or a low molecular weight
agent by a chemical or genetic engineering means.

43. An inhibitor of migration of a monocyte and/or
a macrophage, which comprises, as an active ingredient, a
25 substance which inhibits signal transduction via a human
VEGF receptor Flt-1.

44. The inhibitor of migration of a monocyte
and/or a macrophage according to claim 43, wherein the
substance which inhibits signal transduction via a human
5 VEGF receptor Flt-1 is a substance which inhibits binding
of VEGF to an Flt-1 receptor or a substance which inhibits
signal transduction from an Flt-1 receptor.

45. The inhibitor of migration of a monocyte
10 and/or a macrophage according to claim 44, wherein the
substance which inhibits binding of VEGF to an Flt-1
receptor is an antibody against a human VEGF receptor Flt-1.

46. The inhibitor of migration of a monocyte
15 and/or a macrophage according to claim 45, wherein the
antibody against a human VEGF receptor Flt-1 is a
polyclonal antibody or a monoclonal antibody.

47. The inhibitor of migration of a monocyte
20 and/or a macrophage according to claim 46, wherein the
monoclonal antibody against a human VEGF receptor Flt-1 is
an antibody selected from an antibody produced by a
hybridoma, a humanized antibody and antibody fragments
thereof.

48. The inhibitor of migration of a monocyte and/or a macrophage according to claim 47, wherein the antibody produced by a hybridoma is an antibody selected from KM1732, KM1748 and KM1750.

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49. The inhibitor of migration of a monocyte and/or a macrophage according to claim 47, wherein the humanized antibody is an antibody selected from a human chimeric antibody and a human complementarity determining region-grafted antibody.

10 50. The inhibitor of migration of a monocyte and/or a macrophage according to claim 49, wherein the human chimeric antibody is KM2532 or KM2550.

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51. The inhibitor of migration of a monocyte and/or a macrophage according to claim 49, wherein the human complementarity determining region-grafted antibody is an antibody selected from the group consisting of KM8550, KM8551, KM8552, KM8553, KM8554 and KM8555.

20 52. The inhibitor of migration of a monocyte and/or a macrophage according to claim 47, wherein the antibody fragment is an antibody fragment selected from the group consisting of Fab, Fab', F(ab')₂, a single chain

antibody, a disulfide-stabilized Fv and a peptide comprising a complementarity determining region.

53. The inhibitor of migration of a monocyte
5 and/or a macrophage according to any one of claims 45 to 52,
wherein the antibody is an antibody fused with a
radioisotope, a protein or a low molecular weight agent by
a chemical or genetic engineering means.

10 54. A therapeutic agent for diseases related to a
monocyte and/or a macrophage, which comprises, as an active
ingredient, a substance which inhibits signal transduction
via a human VEGF receptor Flt-1.

15 55. The therapeutic agent according to claim 54,
wherein the disease related to a monocyte and/or a
macrophage is an inflammatory disease, a delayed type
hypersensitivity, an arteriosclerosis or a malignant tumor.

20 56. The therapeutic agent according to claim 55,
wherein the substance which inhibits signal transduction
via a human VEGF receptor Flt-1 is a substance which
inhibits binding of VEGF to an Flt-1 receptor or a
substance which inhibits signal transduction from an Flt-1
25 receptor.

57. The therapeutic agent according to claim 56,
wherein the substance which inhibits binding of VEGF to an
Flt-1 receptor is an antibody against a human VEGF receptor
Flt-1.

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58. The therapeutic agent according to claim 57,
wherein the antibody against a human VEGF receptor Flt-1 is
a polyclonal antibody or a monoclonal antibody.

10 59. The therapeutic agent according to claim 58,
wherein the monoclonal antibody against a human VEGF
receptor Flt-1 is an antibody selected from an antibody
produced by a hybridoma, a humanized antibody and antibody
fragments thereof.

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60. The therapeutic agent according to claim 59,
wherein the antibody produced by a hybridoma is an antibody
selected from KM1732, KM1748 and KM1750.

20 61. The therapeutic agent according to claim 59,
wherein the humanized antibody is an antibody selected from
a human chimeric antibody and a human complementarity
determining region-grafted antibody.

25 62. The therapeutic agent according to claim 61,
wherein the human chimeric antibody is KM2532 or KM2550.

63. The therapeutic agent according to claim 61,
wherein the human complementarity determining region-
grafted antibody is an antibody selected from the group
5 consisting of KM8550, KM8551, KM8552, KM8553, KM8554 and
KM8555.

64. The therapeutic agent according to claim 59,
wherein the antibody fragment is an antibody fragment
10 selected from the group consisting of Fab, Fab', F(ab')₂, a
single chain antibody, a disulfide-stabilized Fv and a
peptide comprising a complementarity determining region.

65. The therapeutic agent according to any one of
15 claims 57 to 64, wherein the antibody is an antibody fused
with a radioisotope, a protein or a low molecular weight
agent by a chemical or genetic engineering means.